OP105 - FILGOTINIB, A SELECTIVE JAK1 INHIBITOR, INDUCES CLINICAL REMISSION IN PATIENTS WITH MODERATE-TO-SEVERE CROHN'S DISEASE: FINAL ANALYSIS OF THE PHASE 2 FITZROY STUDY

16:21-16:33

Severine Vermeire (Belgium) Stefan Schreiber (Germany)
R. Petryka (Poland) Tanja Kuehbacher (Germany)
Xavier Hebuterne (France) Xavier Roblin (France)
Maria Klopocka (Poland) Adrian Goldis (Romania)
Maria Wisniewska Jarosinska (Poland)
Andrey Baranovsky (Russian Federation) Robert Sike (Hungary)
Kremana Stoyanova (Bulgaria) Chantal Tasset (Belgium)
Annegret Van der Aa (Belgium) Pille Harrison (Belgium)

Introduction

Filgotinib is an oral, selective Janus kinase 1 (JAK1) inhibitor, which has demonstrated high efficacy in patients with rheumatoid arthritis. This 20-week Phase 2 study was designed to evaluate the efficacy and safety of filgotinib in patients with active Crohn's disease (CD).

Aims & Methods

174 patients with moderate-to-severe CD (CDAI: 220 to 450, endoscopic evidence of active disease) were randomized 3:1 to receive 200mgfilgotinib (FIL) or placebo (PBO) QD for 10 weeks. Based on Week 10 clinical response, patients continued to receive filgotinib (200mg or 100mg QD) or placebo for an additional 10 weeks. Patients who demonstrated clinical response (CDAI-100) underwent corticosteroid tapering after Week 10. Anti-TNF-naïve as well as anti-TNF non-responders were included. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of clinical remission (CDAI < 150) at Week 10 are presented.

Results

Baseline characteristics were comparable in both groups, including mean disease duration (8.3 y), mean CDAI score (293), mean CRP (15.6 mg/L, 41% > 10mg/L), oral corticosteroids (51%, mean daily dose 21.6 mg/day).

Primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of the patients, compared to 23% in placebo recipients (p= 0.0077), and led to improvement in PRO2 score, and quality of life (IBDQ changes from baseline) compared to placebo (table 1). Numerically more patients

on filgotinib normalized CRP (FIL:27%, PBO:14%) and showed an improvement of at least 50% in SES-CD endoscopy score (FIL:25%, PBO:13.6%), Histopathology overall total score was decreased more significantly in the filgotinib group compared to placebo ($p<0.05$).

Table 1: Key efficacy parameters

Variable/unit/population	**Placebo n=44**	**filgotinib n=128**	**p-value**
Clinical remission (CDAI<150), %, ITT-NRI	23	47	0.0077
PRO2, mean change from baseline, ITT-LOCF	-15.6	-21.9	0.0321
Total IBDQ score, mean change from baseline, ITT-LOCF	17.6	33.8	0.0045
SES-CD improvement by at least 50%, %, ITT-LOCF	13.6	25	NS
overall total histopathology score, mean change from baseline, ITT-LOCF	-0.6	-3.5	0.0359

CDAI: Crohn's Disease Activity Index; ITT: Intent-to-treat; NRI: Non-responder imputation; LOCF: Last observation carried forward; PRO2: Patient Reported Outcome = 7x (mean daily number of liquid or very soft stools) + 7x (mean daily abdominal pain score); IBDQ: Inflammatory Bowel Disease Questionnaire; SES-CD: Simple Endoscopic Score for Crohn's Disease; Histopathology score = Adaptation from histopathology score D'haens

Overall, filgotinib was safe and well tolerated. Similar incidences in early discontinuations, SAEs and AEs including infections were observed, with the majority of the SAEs related to worsening of CD. An increase in mean haemoglobin concentration was observed, without difference betweenfilgotinib and placebo. No clinically significant changes from baseline in mean neutrophil counts or liver function tests were observed. Filgotinibshowed a favourable lipid profile with an increase in HDL and no change in LDL, resulting in an improved atherogenic index.

Conclusion

Inhibition of JAK1 with filgotinib induces clinical remission, supported by CRP, endoscopy and histopathology results, and improves quality of life in patients with moderate to severe CD. The efficacy and safety data offilgotinib suggest a favourable risk/benefit profile, showing its potential as an oral treatment with a novel mechanism of action for the treatment of CD.